REMARKS

Entry of the foregoing and reexamination and reconsideration of the above-captioned application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, in light of the following remarks, are respectfully requested.

Claims 22, 25-27, 30-33, 83, 86, 88, 91, 93, 94, and 105 were pending. Through this amendment, claims 22, 30, 31, 33, and 100 have been amended and claim 26 was canceled. All the other claims remain pending and unamended.

The undersigned wishes to extend his appreciation to the Examiner and the Examiner's supervisor for the courtesy extended by them during a telephone interview held on September 7, 2007. At that interview, applicants' representatives (the undersigned and Mr. Cohen) discussed a draft version of this amendment, which was communicated to the Examiner in preparation for the interview, as well as a table that was faxed the day prior to the interview. In particular, applicants' representatives discussed the support for this amendment and how it further tied the arguments applicants were making in favor of patentability to the data previously presented and to the claims.

During that interview, the Examiners indicated that the *Streisand* reference was not an essential part of the rejection but that the rejection came mainly from the combination of *McCarty* and *Wehling*. Indeed, the Examiner's supervisor indicated that they would consider an additional rejection predicated on *Wehling* as the primary reference and *McCarty* as the secondary reference. Applicants also informed the Examiner and her supervisor that they would be submitting an additional Information Disclosure Statement which accompanies this amendment.

I. OBVIOUSNESS-TYPE DOUBLE PATENTING

The claims of the instant application have been provisionally rejected as being subject to obviousness-type double patenting over co-pending Serial Nos. 11/026,132; 11/027,353; and 11/511,098. Applicants wish to make the Examiner aware that there are additional applications containing related subject matter: Serial Nos. 11/026,327 and 11/026,759, both filed December 30, 2004; and 11/521,796, filed September 15, 2006. In addition, this family includes U.S. Patent Nos. 6,200,604 and 6,974,590. In any event, the claims of the instant application and the claims of the other pending cases are still undergoing examination on the merits and their final scope and content are not ascertainable at this point. Applicants shall determine the appropriateness of filing a terminal disclaimer for the instant application at such time as an indication of allowability of claims is received in this case.

II. OBVIOUSNESS

A. *McCarty* In View Of *Wehling*

The table below, a copy of which was provided to the Examiner and her supervisor on the day prior to the interview, summarizes many of the deficiencies of each of the references applied individually.

Claimed Invention	Reference Relied on by the Office			
Element	*McCarty*	*Wehling*	*Streisand*	*Chen*[1]
Oral Transmucosal Tablet	✓	NO	NO (it is a solution)	✓
Effervescent Couple	NO	✓	NO (it is a solution)	NO
pH Adjusting Substance	NO	NO	✓	NO
Base	NO	NO	✓	NO
Conventional Disintegration Agents	NO (teaches away)	✓	NO (it is a solution)	✓

As is vividly illustrated by the table above, *McCarty* is deficient in almost every aspect of the claimed invention other than it discloses that the claimed active can be administered through an oral transmucosal tablet. In addition to discussing these deficiencies and the lack of any reason on the record to modify *McCarty* with the secondary references, the arguments offered by applicants at the interview were also directed to the fact that the *McCarty* reference actually teaches away from the claimed combination and thus precludes the use of elements described in those secondary references.

Specifically, applicants noted that *McCarty* distinguishes the possibility of using conventional disintegrants in buccal dosage forms, and then, predictably in view of the background, chooses not to use them. *McCarty* clearly advocates that by the use of the sugars it describes, it obtains rapid delivery in an unexpected manner. The Examiners responded that nothing in *McCarty* explicitly teaches away from the use of such disintegrants and therefore it is not a teaching away.

[1] Not established as prior art; upon applicants further reading, *Chen* does not disclose use of methyl cyanide in its formulation, and applicant withdraws that argument.

With all due respect, that is an unfair reading of the reference. At column 1, line 48, *McCarty* describes two types of buccal formulations as being known. One provides sustained release of an active, thereby avoiding swallowing. The other utilizes a disintegrant to accelerate buccal tablet disintegration. (*McCarty* col.1 ll.51-52.) *McCarty* then describes such disintegrants as including PVP, sodium starch glycolate and the like.

In the following paragraph, *McCarty* describes the fact that *McCarty* has discovered a fast buccal formulation which rapidly delivers the active through the buccal route in an "unexpected manner." It then goes on to explain that "manner." A review of column 2 shows that the fast dissolving buccal formulations include three components: the active, which must be buccally absorbable; a pharmaceutically acceptable lubricant; and a directly compressible tablet excipient. While this list does not expressly exclude other possible materials, the only materials which *McCarty* goes on to describe are those three. The examples further emphasize these points as they include only those materials and specifically identify the active, a lubricant and 98.8%w/w of sorbitol.

It is applicants' position that any fair reading of this disclosure is that the "unexpected manner" of achieving fast dissolving buccal formulations in accordance with *McCarty* involved the use of 90% or greater of selected sugars. This was to be distinguished from other buccal formulations which used disintegrants to "accelerate buccal tablet disintegration." *McCarty* acknowledged that disintegrants were used to accelerate buccal tablet disintegration and then, by both word, and through the examples, taught that the use of certain directly

compressible water soluble sugars should replace the use of such disintegrants.[2]

Having taught away from the use of such disintegrants, *Wehling*, which not only discloses the use of such disintegrants but also the use of an effervescent couple, another conventional disintegrant, can only be thought of as the antithesis of the teaching of *McCarty*. With all due respect, *McCarty* teaches away from the very use of such disintegrants taught by *Wehling* and is not combinable therewith.

But this is not the only reason why one of ordinary skill in the art would not look to *Wehling* for combination with *McCarty*. As the Patent Office is well aware, one cannot merely pick and choose elements from individual references for combination. One must consider the totality of the references — the teachings which would invite combination as well as those which would preclude it. *Wehling* is a patent directed to taste masking. It is predicated on the discovery that a rapidly disintegrating tablet, one where the active is preferably further encapsulated to prevent exposure of the active and dissolution in the mouth, can facilitate rapid ingestion without exposure to the adverse taste of the active ingredient.

This is distinguishable from *McCarty* in two very important ways (in addition to *McCarty*'s teaching away of the use of disintegrants as discussed above). First, while *McCarty* is directed to a buccal tablet, *Wehling* is directed to a tablet

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[2] At the interview, the Examiner suggested that perhaps the sugars of *McCarty* were conventional disintegrants. First, it is worthy of note that many of the disintegrants identified in *McCarty* are water insoluble, as opposed to the sugars, which are all characterized as being soluble and *McCarty* requires them to be soluble. Sodium starch glycolate is listed in the *Handbook of Pharmaceutical Excipients* (5th ed.) as being practically insoluble in water. Carboxymethylcellulose is dispersible in water to form a colloidal solution and its crosslinked counterpart is water insoluble. The same is generally true for PVP (water soluble) and its crosslinked counterpart (insoluble). Alginic acid is insoluble in water. Starch is also listed as being practically insoluble in water. Second, it is clear that to *McCarty*, its sugars were not conventional disintegrants.

which is to be swallowed. These are art recognized distinctions and the criteria by which one tablet is designed can bear little resemblance to those used in designing the other. For example, the definition of the active in *Wehling* underscores this point, as *Wehling* contemplated drugs that enter the bloodstream through the stomach or intestines, not the mouth. (*See* WO 91/04757 at 9 ll.14-17.)

Second, *McCarty* recognizes that the active ingredient used must be "buccally absorbable." (*McCarty* col.2 l.9.) However, the actives in accordance with *Wehling* are never intended to dissolve in the mouth, *i.e.*, to be exposed to the taste buds. Indeed, they are to be delivered to the rest of the digestive tract and are preferably encapsulated for taste masking purposes. The encapsulant retards the dissolution of the active in the mouth and therefore the exposure of the taste buds to the objectionable flavor thereof. Rather than providing for a formulation which "rapidly delivers the active ingredient through the buccal route" and requires dissolution of the active in the mouth (col.1 ll.62-3), as desired by *McCarty*, the use of *Wehling* would not have been considered for combination as it clearly attempts to prevent in-mouth exposure of the active.

It is respectfully submitted in view of the foregoing that there is simply no way to combine the disclosures of *Wehling* into *McCarty* without both improperly picking and choosing from *Wehling* only those disclosures deemed necessary for the rejection, which is impermissible, or without fundamentally changing *McCarty* into, at best, a buccal formulation which slowly delivers its active, if not as a swallow tablet, chock full of the very disintegrants *McCarty* sought to avoid.

And this is by no means the only problem with this proposed combination of references. As amended herein, the amount of non-effervescent disintegrant used is up to about 20%. However, *McCarty* teaches the use of between about 90 and about 99% of its

sugar. Nothing in *Wehling* describes using that amount of sugar. Moreover, nothing in *McCarty* suggests that, even if it were possible to replace its sugar with a disintegrant, the amount of a disintegrant used should be 20% or below, as opposed to 90% or above.

And even if *McCarty* and *Wehling* are combined which, for the reasons discussed above, it is applicants' position is improper, nothing in either reference teaches or suggests the use of a pH adjusting substance, let alone a basic pH adjusting substance in combination with fentanyl, as well as its use in combination with an effervescent couple. Finally, nothing suggests that the advantages obtained by the use of the present invention were in any way attainable — that the use of effervescents in combination with a pH adjusting substance is better than the use of either alone.

B. *Wehling* In View Of *McCarty*

At the interview, the supervisory patent Examiner suggested that consideration would be given to a rejection predicated on *Wehling* as the principal reference. The undersigned asked if it would be appropriate to comment on that possibility, even if it were not a formal rejection at this time, in an effort to save time and reduce the number of issues prior to allowance or appeal. With the Examiner's consent, therefore, applicants will address *Wehling* as a primary reference in combination with *McCarty*. With all due respect, while the arguments may change slightly from those offered above, the result should nevertheless be the same.

Unlike *McCarty*, *Wehling* does not teach away from the use of conventional disintegrants. Moreover, it does describe the use of an effervescent couple in combination with those disintegrants. However, that *McCarty* teaches away from the use of disintegrants prevents the combination no less when it is a

secondary reference than when it is a primary reference. Moreover, *Wehling* discloses a tablet designed to be disintegrated in the mouth and be swallowed. How could one combine the teachings of *McCarty* and *Wehling* so as to arrive at a buccal tablet without destroying the very nature and purpose of *Wehling*, something specifically precluded under M.P.E.P. § 2143.01(VI)? The answer is clearly that it cannot. Trying to convert *Wehling* into a buccal tablet is simply not permitted via the combination with *McCarty* or otherwise.

Moreover, and as previously argued above, an essential part of the *Wehling* invention is that the active not be available in the mouth so as to negatively affect taste. Indeed, *Wehling* suggests the use of a coating which provides taste masking in a preferred embodiment. This essential element of *Wehling* is completely inconsistent with *McCarty*'s requirement of a buccally absorbable active ingredient. Since the deficiencies of *Wehling* and *McCarty* are not cured by the secondary references, applicants respectfully submit that the rejection is untenable and should be withdrawn.

And again, even if combined, there would still not be a teaching to use a pH adjusting substance, particularly a basic pH adjusting substance, in a tablet or that such a combination could provide better results than the use of either alone.

Although not discussed extensively at the interview, the *Chen* reference suffers from many of the same deficiencies previously noted. It does not teach the use of an effervescent couple, a pH adjusting substance specifically a base, or the use of a combination of an effervescent couple and a pH adjusting substance. In fact, *Chen* includes carbopol in all of its formulations and acknowledges that carbopol is an "acidic substrate" (p.10 ¶1) and thus contrary to the requirements of the instant claims.

Should the Examiner have any questions with regard to the foregoing, she is encouraged to contact the undersigned at her convenience at (908) 518-6313 in order to overcome any additional objections.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

In view of the foregoing, further and favorable action in the form of a notice of allowance is believed to be next in order and such action is earnestly solicited.

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Respectfully submitted,

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